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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,686	02/14/2002	James G. Boyd	PC23001A	2658

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 05/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,686	BOYD ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150 (CCPA 1977) and have been adopted by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. With respect to (1), the nature of the invention is a compound to be used in treating Alzheimer's disease, Crutzfield-Jacob's disease, prion disorders, amyotrophic lateral sclerosis, progressive supranuclear palsy, head trauma, stroke, Down's syndrome, pancreatitis, inclusion body myocitis, other peripheral amyloidoses and diabetes in a mammal. With respect to (2), there is no effective palliative or preventive treatment for the inevitable neurodegeneration of Alzheimer's disease (see the WO Patent Application 01/00665, page 1, second paragraph). No compound has been developed that significantly affects the course of Alzheimer's disease (see the Potter et al article, Nature Biotechnology, Vol. 18, page 125, column 1, first paragraph).

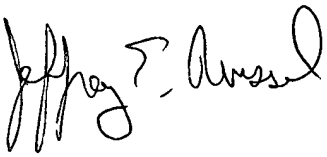
Memapsin 2/BACE-1 is a "potential" target for inhibitor drugs against Alzheimer's diseases (see the Hong et al article, Science, Vol. 290, especially page 150, column 3), but there is no indication that this disease is a potential target for inhibitor drugs against any other disorder or condition claimed by Applicants. There is no compound of similar structure which has been used to treat any of the disorders or conditions claimed by Applicants. With respect to (3), the relative skill of those in the art is high. With respect to (4), the art is not able to predict whether a compound can be used to treat the diseases mentioned in (1) above in the absence of any experimental testing. As indicated by the Potter et al article (Nature Biotechnology, Vol. 18, page 126, column 2, last paragraph, through column 3), the mere in vitro identification of an inhibitor to BACE does not in and of itself establish that the inhibitor can be used in vivo to treat Alzheimer's disease. With respect to (5), the claims are relatively broad with respect to the diseases to be treated. The diseases to be treated, with the exception of Alzheimer's disease, are not caused by the enzyme which is to be inhibited by the claimed compound. There is no common biochemical mechanism which underlies the claimed disorders or conditions such that a treatment useful for treating one condition or disorder would have been expected to be useful in treating the other conditions or disorders. With respect to (6), no direction or guidance has been presented as to how the claimed compound can be used to treat Alzheimer's disease in vivo (see the Potter et al article discussed above) or as to how an enzyme inhibitor can be used to treat disorders or conditions which do not involve the enzyme which is to be inhibited by the compound. For example, the Vassar et al article (Science, Vol. 286, page 739, column 2, last paragraph) teaches that BACE is expressed at higher levels in neurons than in glia. The specification does not disclose how BACE inhibitors can be used to treat disorders or conditions

which do not involve neurons which are expressing BACE, e.g., in the treatment of prion disorders, head trauma, Down's syndrome, and diabetes. With respect to (7), there are no working examples in the application, in vitro or in vivo or otherwise, which show that the claimed compound has any activity. There is a single statement, at page 10, lines 19-20, of the specification, that the claimed compound binds to the enzyme with an IC_{50} equal to $49x10^{-9}M$ as measured by an in-vitro ELISA assay. However, there is no discussion as to how this assay was performed, and in the absence of details of the experimental procedure involved, it is not possible to conclude that the assay is reasonably predictive of in vivo success. With respect to (8), the quantity of experimentation necessary in order to use the invention would be vast, given the lack of any experimentation provided in the specification, given the wide range of disorders and conditions which are to be treated in the claimed invention, and given the current lack of success in treating Alzheimer's disease. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

2. Claims 1-15 are novel and unobvious over the prior art of record or any combination thereof. The prior art of record does not teach or suggest a compound having a structure the same as or similar to that specified in instant claim 1. Accordingly, compositions comprising the compound and methods of using the compound are also novel and unobvious over the prior art of record.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

May 14, 2003